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conserved across at least two species comprising the sequence NNNGAUNCUUUNNGUAAGC CCNANGNGNN (SEQ ID NO:23).

111. (Amended twice) A purified and isolated RNA fragment up to 70 nucleotides comprising the human sequence UAUGAUUCUUUUUGUAAGCCCUAGGGGCU (SEQ ID NO:24).

112. (Amended twice) A purified and isolated RNA fragment up to 70 nucleotides comprising the mouse sequence AAAGAUUCUUUUUGUAAGCCCCAAGGGCU (SEQ ID NO:25).

113. (Amended twice) A purified and isolated RNA fragment up to 70 nucleotides comprising the rat sequence AAAGAUUCUUUUUGUAAGCCCCAAGGGCU (SEQ ID NO:25).

REMARKS

Claims 87-100, 108, and 110-113 are pending in the present application. Claims 94-100 and 108 have been cancelled without prejudice to their presentation in another application. Claims 110-113 have been amended herein. Upon entry of the present amendment, claims 87-93 and 110-113 will remain pending. ***Because the amendments to the claims remove issues for appeal (i.e., anticipation rejections), Applicants respectfully request that they be entered into the record. See, M.P.E.P. § 714.12.***

The specification stands objected to for allegedly embedding references to computer web sites. In response to a previous objection based on the same grounds, the specification was amended to remove hyperlinks/browser-executable code. A web browser would not recognize the amended computer addresses as executable code and, thus, would not view any words or phrase in the specification as a valid World Wide Web link. In particular, the amended specification does not include URLs placed between the symbols "< >" or include "http://" followed by a URL address. Accordingly, Applicants respectfully request that this objection be withdrawn.

I. The Final Rejection Is Premature

The finality of the present Office Action should be withdrawn because the Examiner has introduced a new ground of rejection that was not previously of record in any of the preceding Office Actions. Of particular interest, M.P.E.P. § 706.07(a) states:

> Under present practice, second or any subsequent actions on the merits shall be final, ***except where the examiner introduces a new ground of rejection*** that is neither necessitated by applicant's amendment of the claims nor based on information submitted in an information disclosure statement filed during the period set forth in 37 CFR 1.97(c). (emphasis added)

The Office has introduced a new provisional rejection under the judicially created doctrine of obviousness-type double patenting. This rejection was neither necessitated by an Applicants' amendment nor based on information submitted in an information disclosure statement filed during the period set forth in 37 CFR 1.97(c). Indeed, the obviousness-type double patenting rejection could have been levied in the previous Office Action.

In view of the foregoing, Applicants respectfully request that the finality of the Office Action be withdrawn.

II. The Claimed Invention Is Novel

A. The McKnight Reference

Claims 87-100, 108, 110, 112, and 113 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by McKnight *et al.*, *Immunogenetics.*, **1989**, *30*, 145-47 (hereinafter, the "McKnight reference"). Applicants traverse the rejection and respectfully request reconsideration thereof because the McKnight reference fails to teach every element recited in the claims.

The McKnight reference reports a cDNA sequence of a rat IL-2 clone that contains a 5' untranslated region, coding region, and 3' untranslated region in Figure 1. In total, the reported cDNA sequence contains 740 nucleotides. The McKnight reference fails to teach any secondary structure associated with the 740 nucleotide cDNA sequence.

Regarding claims 87-93, the Office Action incorrectly asserts that the McKnight reference teaches an RNA comprising SEQ ID NO:23 and SEQ ID NO:25 and having at least twenty-nine but

no more than seventy nucleotides, which contains the secondary structure recited in claim 87. Regardless of whether the cDNA sequence reported in the McKnight reference comprises the secondary structure recited in claim 87 (and Applicants submit that the Office Action utterly fails to establish that such secondary structure is inherent in the reported cDNA sequence), the McKnight reference fails to teach an RNA comprising "not more than seventy nucleotides." A prior art reference anticipates a claim if every element of the claim appears in the prior art reference. *Glaxo Inc. v. Novopharm, Ltd.*, 52 F.3d 1043, 1047, 34 U.S.P.Q.2d 1565, 1567 (Fed. Cir. 1995). Because the cDNA sequence reported in the McKnight reference is 740 nucleotides in length, it does not anticipate claim 87 (nor dependent claims 88-93), which recites an RNA "not more than seventy nucleotides."

The Office Action takes the view that due to the use of the word "comprising," the claims read on sequences that are longer than 70 nucleotides. Applicants respectfully disagree and submit that the Examiner cannot consider individual terms recited in a claim and interpret them in a vacuum. Claim 87 states, in part, "An RNA comprising a joined sequence of at least twenty-nine ***but not more than seventy nucleotides*** ..." (emphasis added). Claim 87, therefore, recites that the joined sequence ranges from twenty-nine to seventy nucleotides. The position taken by the Examiner completely vitiates the explicit language recited in the claim. The term "comprising" relates to other components of the RNA that do not involve the overall number of nucleotides in the sequence. Indeed, an RNA that has forty nucleotides and the secondary structure recited in claim 87 in addition to, for example, a radiolabel would infringe claim 87. Thus, the McKnight reference does not disclose an RNA that comprises a joined sequence of "at least twenty-nine but not more than seventy nucleotides" and, therefore, does not anticipate the claimed inventions.

Claims 94-100 and 108 recite an RNA having a particular secondary structure. It is undisputed that the McKnight reference fails to disclose any secondary structure of the 740 nucleotide cDNA sequence reported therein. Nonetheless, the Office Action assumes that the McKnight cDNA comprises the secondary structure recited in claims 94-100 and 108. Thus, it appears that the Office Action asserts that the secondary structure recited in Applicants' claims is inherent in the McKnight cDNA sequence. To anticipate a claim, however, a prior art reference must

disclose every feature of the claimed invention, either explicitly or inherently. *Glaxo v. Novopharm, Ltd.*, 334 U.S.P.Q.2d 1565 (Fed. Cir. 1995). Further, to serve as an anticipation when a reference is silent about the alleged inherent characteristic, such gap in the reference may be filled by extrinsic evidence. Such evidence, however, must make clear that the missing descriptive matter is necessarily (*i.e.*, always) present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill in the art. *In re Oelrich*, 40 U.S.P.Q. 323 (C.C.P.A. 1981); *Continental Can Co. USA Inc. v. Monsanto Co.*, 20 U.S.P.Q.2d 1746 (Fed. Cir. 1991). Inherency may not be established by probabilities or possibilities. *Id.* Further, the mere fact that a certain thing may result from a given set of circumstances is not sufficient. *Id.* Significantly, the Office Action has not established that the critical inherent characteristics are necessarily present in the McKnight reference. Indeed, the Office Action fails to provide any extrinsic evidence that makes clear that the missing descriptive matter is always present in the thing described in the McKnight reference, and that it would be so recognized by persons of ordinary skill in the art. To advance prosecution of the present application, however, claims 94-100 and 108 have been cancelled without prejudice to their presentation in another application.

Claims 110, 112 and 113 recite an "RNA fragment." In contrast, the McKnight reference reports a cDNA sequence containing the 5' untranslated region, coding region, and 3' untranslated region -- *i.e.*, a cDNA containing the entire gene. Aside from the fact that the sequence reported in Figure 1 of the McKnight reference is a cDNA sequence and not a "purified and isolated RNA," it is also not a "fragment." A reference that requires picking and choosing among options disclosed in the reference to such a degree that one skilled in the art would not recognize the claimed invention does not anticipate the claimed invention. *See In re Arkley*, 172 U.S.P.Q. 524, 526 (C.C.P.A. 1972); *In re Ruschig*, 145 U.S.P.Q. 274, 282 (C.C.P.A. 1965). In the present case, the McKnight reference does not even present Applicants' claimed inventions as options. In addition, the Office Action fails to assert, let alone prove, that the McKnight sequence is "conserved across at least two species," as recited in claim 110. Thus, the McKnight reference also fails to anticipate claims 110, 112, and 113. Applicants direct the Examiner's attention to the discussion above regarding the term "comprising" and submit that the McKnight reference nowhere teaches a "fragment" comprising the recited

sequences. To advance prosecution of the present application, claims 110, 112, and 113 have been amended to recite "up to 70 nucleotides," support for which can be found, for example, at page 152, lines 6-8 of the specification as filed.

In view of the foregoing, the McKnight reference fails to anticipate claims 87-93, 110, 112 and 113. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 102(b) be withdrawn.

B. The Chen Reference

Claims 87-100, 108, 110, and 111 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Chen *et al.*, *Proc. Natl. Acad. Sci. USA,* **1985**, *82*, 7284-7288 (hereinafter, the "Chen reference"). Applicants traverse the rejection and respectfully request reconsideration thereof because the Chen reference fails to teach every element recited in the rejected claims.

The Chen reference reports a cDNA sequence of a human IL-2 clone and two gibbon IL-2 clones that contains a 5' untranslated region, coding region, and 3' untranslated region in Figure 3. In total, the reported cDNA sequences each contain from about 800 to 1000 nucleotides. The Chen reference fails to teach any secondary structure associated with the cDNA sequences reported therein.

In regard to claims 87-93, in similar fashion to the rejection over the McKnight reference, the Office Action incorrectly asserts that the Chen reference teaches an RNA comprising SEQ ID NO:24 and having at least twenty-nine but no more than seventy nucleotides, which contains the secondary structure recited in claim 87. Regardless of whether the cDNA sequences reported in the Chen reference comprise the secondary structure recited in claim 87 (and Applicants submit that the Office Action utterly fails to establish that such secondary structure is inherent in the reported cDNA sequences), the Chen reference fails to teach an RNA comprising "not more than seventy nucleotides." As stated above, a prior art reference anticipates a claim if every element of the claim appears in the prior art reference. Because the cDNA sequences reported in the Chen reference are at least 800 to 1000 nucleotides in length, it does not anticipate claim 87 (nor dependent claims 88-93), which recites an RNA "not more than seventy nucleotides." Further, as discussed above, use of the

term "comprising" in the claims does not vitiate the phrase "at least twenty-nine but not more than seventy nucleotides."

Claims 94-100 and 108 recite an RNA having a particular secondary structure. It is undisputed that the Chen reference fails to disclose any secondary structure of the at least 800 nucleotide cDNA sequences reported therein. Nonetheless, the Office Action assumes that the Chen cDNA comprises the secondary structure recited in claims 94-100 and 108. Thus, it appears that the Office Action asserts that the secondary structure recited in Applicants' claims is inherent in the Chen cDNA sequence. As stated above, to anticipate a claim, a prior art reference must disclose every feature of the claimed invention, either explicitly or inherently, and any gaps may be filled by extrinsic evidence. Significantly, the Office Action has not established that the secondary structure recited in the claims is necessarily present in the Chen reference. Indeed, the Office Action fails to provide any extrinsic evidence that makes clear that the missing descriptive matter is always present in the thing described in the Chen reference, and that it would be so recognized by persons of ordinary skill in the art. Thus, Office Action has failed to establish that the Chen reference anticipates claims 94-100 and 108. To advance prosecution of the present application, however, claims 94-100 and 108 have been cancelled without prejudice to their presentation in another application.

Claims 110 and 111 recite an "RNA fragment." In contrast, the Chen reference reports cDNA sequences containing the 5' untranslated region, coding region, and 3' untranslated region -- *i.e.*, cDNAs containing the entire gene. Aside from the fact that the sequence reported in Figure 3 of the Chen reference is a cDNA sequence and not a "purified and isolated RNA," it is also not a "fragment." As stated above, a reference that requires picking and choosing among options disclosed in the reference to such a degree that bone skilled in the art would not recognize the claimed invention does not anticipate the claimed invention. The Chen reference fails to particularly point out nucleotides 650 to 678. Indeed, Applicants' specification provides the only basis for selecting a fragment comprising the recited nucleotide sequence. Further, in the present case, the Chen reference does not even present Applicants' claimed inventions as options. Thus, the Chen reference also fails to anticipate claims 110 and 111. Applicants direct the Examiner's attention to the discussion above

regarding the term "comprising" and submit that the Chen reference nowhere teaches a "fragment" comprising the recited sequences. To advance prosecution of the present application, claims 110 and 111 have been amended to recite "up to 70 nucleotides," support for which can be found, for example, at page 152, lines 6-8 of the specification as filed.

In view of the foregoing, the Chen reference fails to anticipate claims 87-93, 110, and 111. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 102(b) be withdrawn.

C. The Fu Reference

Claims 87-91, 94-98, 108, 110, 112, and 113 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 6,090,620 (hereinafter, the "Fu reference"). Applicants traverse the rejection and respectfully request reconsideration thereof because the Fu reference fails to teach every element recited in the rejected claims.

The Examiner continues to assert that the Fu reference teaches genomic DNA encoding the WRN gene, which encodes RNA comprising SEQ ID NOs:23 and 25, having at least twenty-nine but not more than seventy nucleotides. The only sequence within the Fu reference that the Examiner specifically identifies is nucleotides 26015 to 26041 within SEQ ID NO:209, which is AGTTTCTTTTTGGAAGCACTTAGAGCT and which is only twenty-seven nucleotides in length. SEQ ID NO:209 reported in the Fu reference is 51,259 nucleotides long.

In regard to claims 87-91, in similar fashion to the rejections over the McKnight and Chen references, the Office Action incorrectly asserts that the Fu reference teaches an RNA comprising SEQ ID NOs:23 and 24, and having at least twenty-nine but no more than seventy nucleotides, which contains the secondary structure recited in claim 87. Regardless of whether the DNA sequence reported in SEQ ID NO:209 of the Fu reference comprises the secondary structure recited in claim 87 (and Applicants submit that the Office Action utterly fails to establish that such secondary structure is inherent in the reported DNA sequence), the Fu reference fails to teach an RNA comprising "not more than seventy nucleotides." As stated above, a prior art reference anticipates a claim if every element of the claim appears in the prior art reference. Because the DNA sequences reported in the

Fu reference contains more than 50,000 nucleotides, it does not anticipate claim 87 (nor dependent claims 88-91), which recites an RNA "not more than seventy nucleotides." Further, it is not even clear how the cited portion of the genomic DNA sequence reported in SEQ ID NO:209 of the Fu reference encodes RNA comprising SEQ ID NOs:23 and 25. Further, as discussed above, use of the term "comprising" in the claims does not vitiate the phrase "at least twenty-nine but not more than seventy nucleotides."

Claims 94-98 and 108 recite an RNA having a particular secondary structure. It is undisputed that the Fu reference fails to disclose any secondary structure for the 50,000+ nucleotide sequence of SEQ ID NO:209 or the cited portion thereof. Nonetheless, the Office Action assumes that the Fu DNA comprises the secondary structure recited in claims 94-98 and 108. Thus, it appears that the Office Action asserts that the secondary structure recited in Applicants' claims is inherent in the Fu DNA sequence. As stated above, to anticipate a claim, a prior art reference must disclose every feature of the claimed invention, either explicitly or inherently, and any gaps may be filled by extrinsic evidence. Significantly, the Office Action has not established that the secondary structure recited in the claims is necessarily present in the Fu reference. Indeed, the Office Action fails to provide any extrinsic evidence that makes clear that the missing descriptive matter is always present in the thing described in the Fu reference, and that it would be so recognized by persons of ordinary skill in the art. Thus, Office Action has failed to establish that the Fu reference anticipates claims 94-98 and 108. To advance prosecution of the present application, however, claims 94-98 and 108 have been cancelled without prejudice to their presentation in another application.

Claims 110, 112 and 113 recite an "RNA fragment." In contrast, the Fu reference reports a genomic DNA sequence. Aside from the fact that the sequence reported in SEQ ID NO:209 of the Fu reference is genomic DNA and not a "purified and isolated RNA," it is also not a "fragment." As stated above, a reference that requires picking and choosing among options disclosed in the reference to such a degree that bone skilled in the art would not recognize the claimed invention does not anticipate the claimed invention. Further, in the present case, SEQ ID NO:209 of the Fu reference does not even teach the nucleotide sequences recited in claims 110, 112 and 113. In addition, the Office Action fails to assert, let alone prove, that SEQ ID NO:209 or any portion thereof is

"conserved across at least two species," as recited in claim 110. Thus, the Fu reference also fails to anticipate claims 110, 112 and 113. Applicants direct the Examiner's attention to the discussion above regarding the term "comprising" and submit that the Fu reference nowhere teaches a "fragment" comprising the recited sequences. To advance prosecution of the present application, claims 110, 112 and 113 have been amended to recite "up to 70 nucleotides," support for which can be found, for example, at page 152, lines 6-8 of the specification as filed.

In view of the foregoing, the Fu reference fails to anticipate claims 87-91, 110, 112, and 113. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 102(e) be withdrawn.

III. There Is No Obviousness-Type Double Patenting

Claims 87-100, 108, and 110-113 stand provisionally rejected under the doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 11, 13, 14, and 16 of co-pending Application No. 09/310,735 (hereinafter, the "735 application"). The Office Action alleges that although the conflicting claims are not identical, they are not patentably distinct. Claims 94-100 and 108 have been cancelled without prejudice to their presentation in another application. Applicants traverse the rejection, as it is applied to claims 87-93 and 110-113, and request reconsideration thereof.

An obviousness-type double patenting rejection is analogous to a failure to meet the nonobviousness requirement of 35 U.S.C. § 103. *In re Braithwaite*, 154 U.S.P.Q. 29, 34 (C.C.P.A. 1967) and *In re Longi*, 225 U.S.P.Q. 645, 648 n.4 (Fed. Cir. 1985). Thus, under the law, the pivotal question in an obviousness-type double patenting analysis is: Does any claim in the application define merely an obvious variation of an invention disclosed ***and claimed*** in the patent? *In re Vogel*, 164 U.S.P.Q. 619 (C.C.P.A. 1970) (emphasis added). If the answer to this question is no, there can be no double patenting. In making this analysis, then, the proper inquiry is as taught in *Graham v. John Deere Co.*, 383 U.S. 1 (1966). See, M.P.E.P. §804.

Claims 11, 13, 14, and 16 of the '735 application are drawn to compounds identified by particular methods for identifying compounds that modulate activity of target RNAs or target

biomolecules. The claims of the '735 application do not recite any of the secondary structures, joined sequence length, or nucleotide sequences that are recited in the claims of the present application. Thus, the RNA molecules of the present invention, which recite secondary structures, joined sequence lengths, or nucleotide sequences are not obvious variants of the compounds claimed in the co-pending application, which fail to recite any of these elements.

That an RNA molecule of the present invention may fall within the claim scope of the co-pending application is irrelevant. Indeed, a determination whether one patent application is generic to another patent application is not the appropriate inquiry. The following quotation from *In re Kaplan*, 229 U.S.P.Q. 678 (Fed. Cir. 1986) is instructive:

> By domination we refer ... to that phenomenon ... whereunder one patent has a broad or "generic" claim which "reads on" an invention defined by another narrower or more specific claim in another patent, the former "dominating" the latter because the more narrowly claimed invention cannot be practiced without infringing the broader claim ... In possibly, simpler terms, one patent dominates another if a claim of the first patent reads on a device built or process practiced according to the second patent disclosure. This commonplace situation is not, *per se*, double patenting as the board seems to think. (citations omitted).

Thus, that some of Applicants' compounds claimed in the present patent application may also meet limitations of claims in co-pending patent applications (of which Applicants do not concede) is not grounds for an obviousness-type double patenting rejection. It is simply a case of one patent application dominating another patent application. Domination by itself cannot support a double patenting rejection. Thus, the obviousness-type double patenting rejection is misplaced.

In view of the foregoing, Applicants respectfully request that the rejection of claims 87-93 and 110-113 under the doctrine of obviousness-type double patenting be withdrawn.

IV. Conclusion

In view of the foregoing, Applicants respectfully submit that the finality of the Office Action should be withdrawn, that the amendments to the claims should be entered, and that the claims are in condition for allowance. An early notice of the same is earnestly solicited. The Examiner is invited to contact Applicants' undersigned representative at (215) 564-8906 if there are

any questions regarding Applicants' claimed invention. Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 94-100 and 108 have been cancelled without prejudice to their presentation in another application.

Claims 110-113 have been amended as follows:

110. (Amended twice) A purified and isolated RNA fragment up to 70 nucleotides that is conserved across at least two species comprising the sequence NNNGAUNCUUUNNGUAAGC CCNANGNGNN (SEQ ID NO:23).

111. (Amended twice) A purified and isolated RNA fragment up to 70 nucleotides comprising the human sequence UAUGAUUCUUUUUGUAAGCCCUAGGGGCU (SEQ ID NO:24).

112. (Amended twice) A purified and isolated RNA fragment up to 70 nucleotides comprising the mouse sequence AAAGAUUCUUUUUGUAAGCCCCAAGGGCU (SEQ ID NO:25).

113. (Amended twice) A purified and isolated RNA fragment up to 70 nucleotides comprising the rat sequence AAAGAUUCUUUUUGUAAGCCCCAAGGGCU (SEQ ID NO:25).